Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 31 (2019) 346–349

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Importance of professional oral hygiene for prevention of aspiration pneumonia caused by progressive central nervous system disorders in Type 2 Gaucher disease

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ARTICLE INFO

Keywords:
Type 2 Gaucher disease

ABSTRACT

Gaucher disease (GD) is rare that is caused by an enzyme deficiency of lysosomal glucocerebrosidase and is one of the most frequent lysosomal storage diseases. We present here the case of an infant male with Type 2 GD (GD2). GD2 is clinically characterized by precocious and rapid neurological degeneration comprising brainstem involvement associated with hepatosplenomegaly, pulmonary and hematological involvements, and death will be in infancy or early childhood. We performed professional oral hygiene on a patient with GD2, and we contributed to the communication between the patient and his family. Here we report on the oral cavity features in GD2 and how our experience can contribute to the prevention of aspiration pneumonia.

1. Introduction

Gaucher disease (GD) is caused by an enzyme deficiency of lysosomal glucocerebrosidase and is one of the most frequent lysosomal storage diseases [1]. GD is classified into three subtypes, type 1, 2, and 3, according to the presence or absence of nervous symptoms and onset of the disease [1]. Type 2 GD (GD2) is clinically characterized by precocious and rapid neurological degeneration comprising brainstem involvement associated with hepatosplenomegaly, pulmonary and hematological involvements such as anemia and thrombocytopenia, and death will be in infancy or early childhood [2]. The frequency of GD2 is about 1/150,000, which is rather common in Japanese people [3]. GD1, which is characterized by various degrees of bone involvements and hepatosplenomegaly without neurological disorder is most common in Jewish people. Intraoral findings [4–6] and oral health [7] in GD1 have been reported previously, but there are few reports of intraoral findings in GD2. We performed professional oral hygiene on a patient with GD2, and we contributed to the communication between the patient and his family. Here we report on the oral cavity features in GD2 and how our experience can contribute to the prevention of aspiration pneumonia.

2. Case report

A male baby was born after an uneventful pregnancy and normal delivery. His weight at birth was 3132 g. after 40 weeks 2 days gestation. There was no family history of medical problems. At 3 months of age, the child began to have difficulty in feeding and a decrease in weight. At 5 months of age, he was suspected to have GD2 because of bulbar paralysis and splenohepatomegaly. At 7 months of age, a diagnosis of GD2 was finally made based on clinical signs and confirmed by low glucocerebrosidase enzyme activity. At 8 months of age, tracheotomy was performed because of increasing spasms of the larynx. At 9 months of age, enzyme replacement therapy (ERT) was started. Hoping for home care, he was transferred to the pediatrics department

Abbreviation: GD, Gaucher disease

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https://doi.org/10.1016/j.ajoms.2019.03.007
Received 30 September 2018; Received in revised form 31 December 2018; Accepted 19 March 2019
Available online 31 August 2019

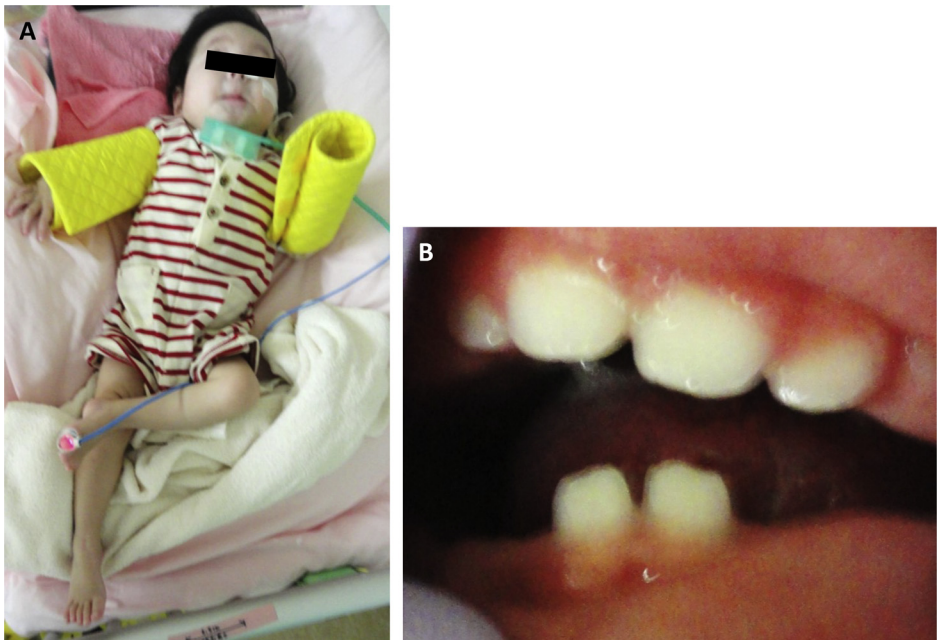

Fig. 1. View of the patient at about 11 months of age, at first visit. A. Opisthotonos as a neurological finding, and he did not have head control. He was given nourishment through a nasogastric tube. B. Erupted teeth were deciduous upper central incisors, lateral incisors and lower central incisors. Mild gingivitis in his oral cavity was seen.

in our hospital. At 10 months of age, his parents desired a massive dose therapy by ambroxol. He underwent GBA genetic testing and a cheaperone test. As a result, gene mutation indicated compound heterozygote mutation in the GBA gene (R120W/L483 P), but we could not prove the efficacy of the administration of ambroxol. At about 11 months of age, the patient was referred to the Department of Oral and Maxillofacial Surgery for the purpose of professional oral hygiene. At that time his weight and length were 7500 g and 69.5 cm (Fig. 1A). His neurological findings showed opisthotonos and esotropia, and he had no head control. His neurological findings showed aphagia, and he was given nourishment through a nasogastric tube. His oral findings showed mild gingivitis. His erupted teeth were the deciduous upper central incisors, lateral incisors and lower central incisors, appropriately for his age. Laboratory tests showed platelet (PLT) count of 14.9×10^4 /μL, Hemoglobin (Hb) value of 10.0 g/ dL (normal range = 10.5–14.1 g/dL); Aspartate Aminotransferase (AST) 88 U/L (normal range = 23–57 IU/L); and Alkaline Phosphatase (ALP) 42U/L (normal range = 395–1339 IU/L) at abnormal values. Angiotensin-converting enzyme (ACE) 110.5 U/L (normal range = 8.0–21 U/L) and Acid phosphatase (ACP) 151.5 U/L (normal range = 5.4–14U/L), which are high in GD, were also high in our patient. Krebs von den L ungen-6 (KL-6) 2363 U/mL (normal range= –1000 U/mL) as a specific interstitial pneumonia marker was also high. The other laboratory tests showed normal levels. A CT scan showed marked brain atrophy (Fig. 2A), and also huge splenohepatomegaly (Fig. 2B); a chest X-ray showed interstitial pneumonia (Fig. 2C).

At 9 months of age, ERT was started with imiglucerase (Cerezyme®) at a dose of 55 U/kg/2 weeks, after which there was an improvement in the non-neurological findings such as hepatosplenomegaly and hematological findings (anemia and thrombocytopenia) plates, but the neurological findings became worse. At 12 months of age, his muscle tone improved and enteral nutrition permited regurgitation into the oral cavity, but he had fever and increasing CRP caused by aspiration pneumonia. Anti-inflammation by antibiotics and an increase in the dosage of the muscle relaxant agent were carried out as symptomatic therapy.

In the oral cavity findings, he had a reduced amount of mouth opening because of brainstem symptoms, and he could not open his mouth at 13 months of age. He did not respond to desensitization and his mouth could not be forcibly opened. His interstitial pneumonia got worse, and he started using a respirator, but at 15 months of age he died of respiratory failure as the primary disease. The number of primary and permanent teeth and germ teeth were normal in a posthumously taken CT, and the shape of the jawbone was normal (Fig. 3).

We performed professional oral hygiene at a few hours intervals after each meal from first visit because prevention of aspiration pneumonia is essential, and we taught his parents how to clean his oral cavity two weeks later. We gave his parents the following oral hygiene instructions and taught them the method of oral care according to the care for patients with central neurological diseases. First, we performed desensitization and release of muscle tension around the mouth after physical therapy rehabilitation (Fig. 4A). Second, we improved his oral mobility by the methods of vangede [8] (Fig. 4B). Third, we gave him gingival massage to develop the function of oral sensation (Fig. 4C). Finally, we cleaned his oral cavity using gauze, a sponge brush, and a toothbrush (Fig. 4D). His parents cooperated in cleaning his oral cavity in each step. Questions from his mother and grandmother about his oral care showed their proactive behavior two months later, leading us to consider that his oral care contributed to the communication between the patient and his family.

3. Discussion

Cyril Mignot et al. reported that trismus as one of the oral cavity findings occurred in an average of 24% of GD2 patients [9], but there is no literature about its pathogenic mechanism. In the present case, trismus appeared at 12 months of age. Apnea occurs in 87% of GD2 patients at 7.7 months of age [8]. Jaw features in GD have been described, but those in GD2 are few, due to death by two years of age [10]. In this case, the patient died at 15 months of age, and he had no jaw lesions such as a cyst.

The β- glucocerebrosidase do not cross the blood-brain barrier, and there is no report that ERT improves the neurological symptoms in patients with GD2 or GD3 [11]. ERT is not beneficial when the primary cause of pulmonary involvement is recurrent aspiration secondary to neurological deterioration, but it is not known whether ERT improves pulmonary involvement [12,13]. ERT can, however, improve the visceromegaly and hematologic abnormalities in patients with GD2 [12,13]. On the other hand, it has been reported that a high dose of ERT is useful for the pulmonary involvement in GD2 [14]. A guideline of ERT for Gaucher disease recommends a dosage of intravenous imiglucerase 15–60 units/kg/2 weeks in the case of GD1. Our patient was administered a dosage of imiglucerase 55 units/kg/2 weeks on the basis

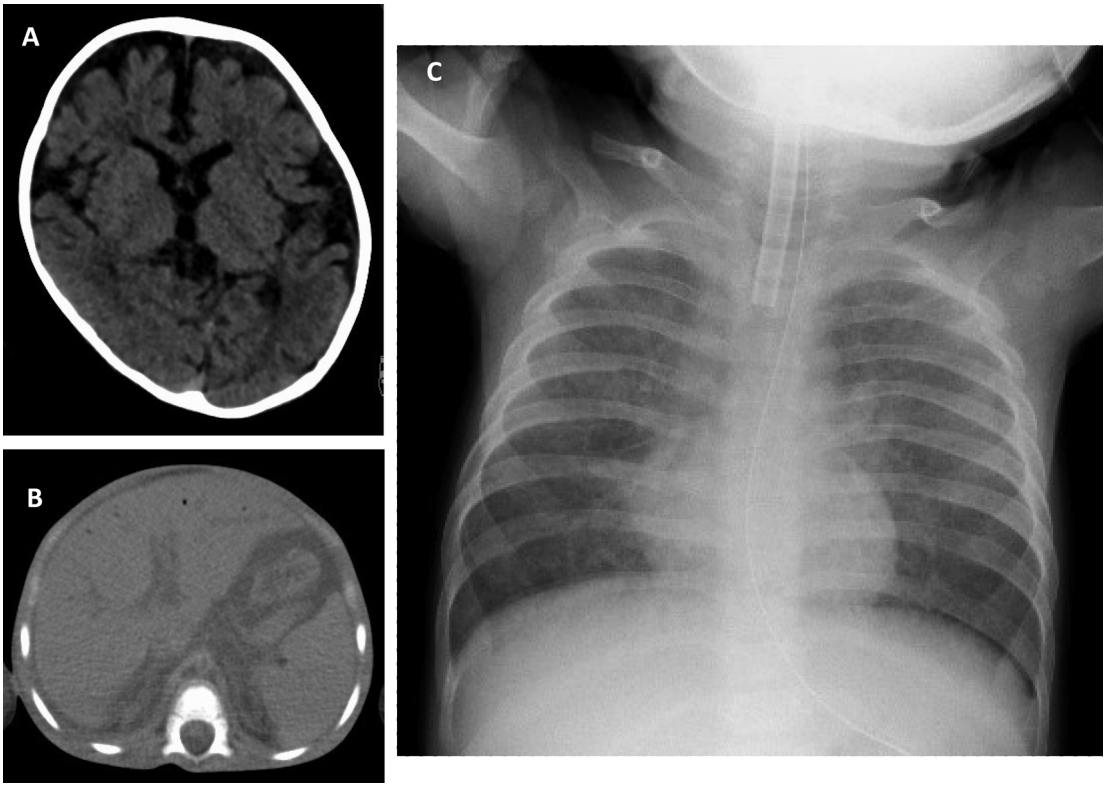

Fig. 2. CT view: A, brain atrophy, B, splenohepatomegalia, Chest X-ray: C, interstitial pneumonia.

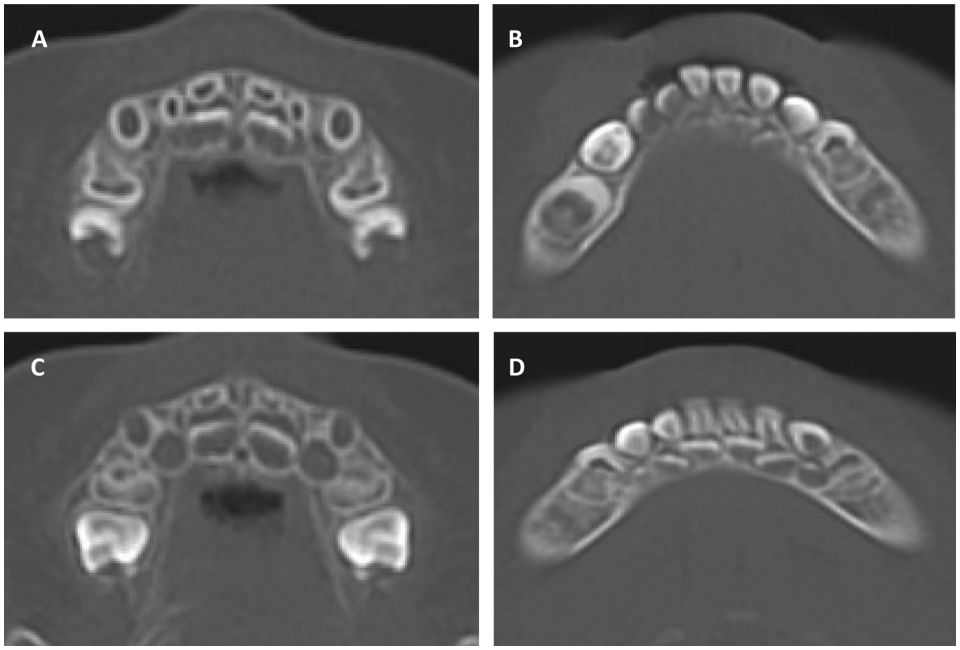

Fig. 3. CT axial sections: the number of baby and permanent teeth and germ teeth was normal, and the shape of the jawbone was normal, too. A, Baby teeth in maxilla; B, Permanent teeth and germ teeth in maxilla; C, Baby teeth in mandible; D, Permanent teeth and germ teeth in the mandible.

of ERT recommendations in Japan. As a result, there was improvement in non-neurological findings such as hepatosplenomegaly and anemia and thrombocytopenia, but the neurological findings became worse.

GBA gene mutation has been reported by Beutler [15] and Tsuji [16] et al., and our gene mutation was also described in their papers.

Pulmonary lesion in GD is caused by infiltration of Gaucher cells to the alveoli and capillaries in the alveolar septum [14], but it is difficult to distinguish pulmonary lesions caused by a primary disease from central apnea and aspiration pneumonia [8]. There are reported that aspiration pneumonia had the potential to encourage pulmonary lesions caused by a primary disease. Mignot et al. reported that half of deaths in GD2 are caused by respiratory failure [8]. In our case, since the patient's muscle tone improved, enteral nutrient permitted regurgitation into the oral cavity, which was followed by fever and an increase of WBC and CRP. Anti-inflammation by antibiotics and an increase in the dosage of a muscle relaxant agent were effective as symptomatic

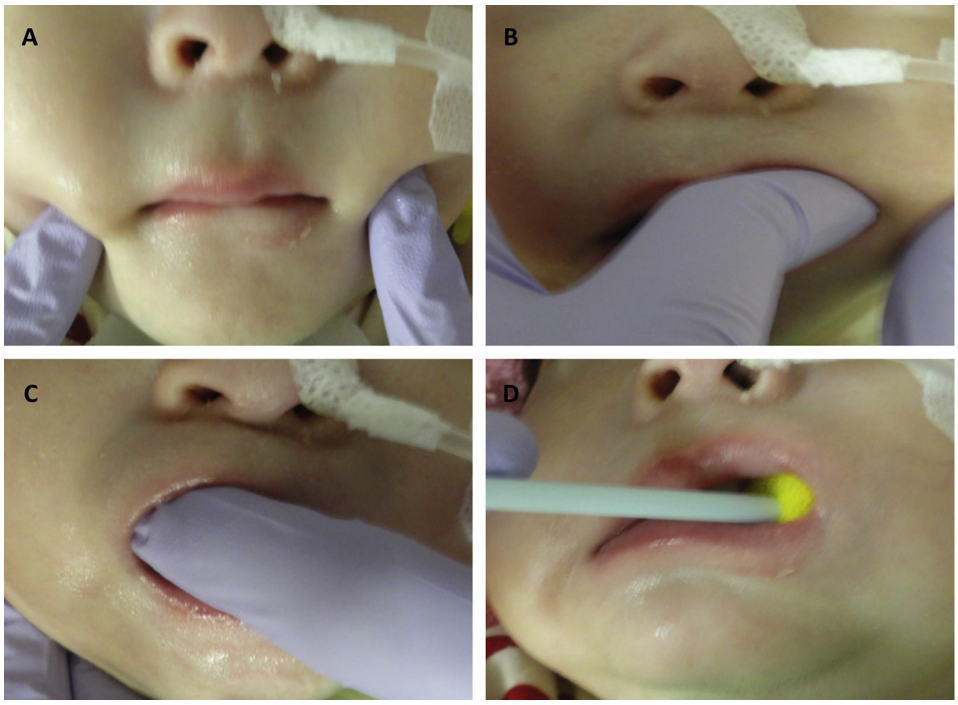

Fig. 4. professional oral care. A, first we performed desensitization and release of muscle tension around the mouth. B, second, we improved his oral mobility by the methods of vangede. C, third, we gave him gingival massage to develop the function of oral sensation. D, finally, we cleaned his oral cavity using gauze, sponge brush, and toothbrush.

therapy, but this resulted in aspiration pneumonia. Finally, through the treatment aspiration pneumonia, WBC and CRP returned to normal levels, but the radiopacity of the lungs increased, and he died from the progression of the pulmonary disease associated with neurological involvement.

4. Conclusion

Taken together, GD2 causes not only pulmonary lesion by the primary disease but also clinical symptoms such as decreased muscle tone, trismus, and dysphagia with progression of central nervous system disorders. We considered that professional oral hygiene in collaboration with the department of pediatrics would be important to prevent aspiration pneumonia caused by progressive central nervous system disorders. Also, GD2 takes a progressive clinical course related to the central nervous system and therefore palliative care for the patient and mental care for the parents are essential [17]. We believe that our patient's oral care contributed to the prevention of pulmonary problems through the communication with the patient's family.

Ethical approval

It was approved by the ethics committee in Shinyurigaoka General Hospital.

Conflict of interest

Authors declare no conflicts of interest associated with this publication.

Acknowledgements

We are grateful to Dr. Eto Yoshikatsu for his guidance in this work.

We wish to thank Dr. Nanba Eiji for his help given by genetic testing.

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